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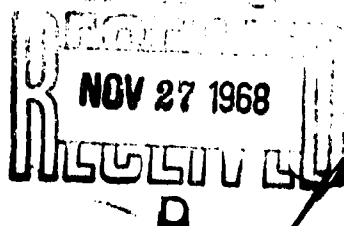
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DEPARTMENT OF THE ARMY  
Fort Detrick  
Frederick, Maryland

RUPTURE OF A BOND WITHIN THE ORGANOMETALLIC  
TRANSITION COMPLEX: ACTIVE AND  
ANTAGONISTIC CATIONS

Following is a translation of an article by  
Mme Andree Goudot, presented at the 19 Decem-  
ber 1960 meeting of the French Academy of  
Sciences and published in the French-language  
periodical Comptes rendus de l'Academie des  
Sciences (Reports of the Academy of Sciences),  
Vol 252, 1961, pages 125-127, under the sub-  
ject heading of Theoretic Chemistry.

Enzymatic reactions activated by metallic cations  
always are produced in accordance with the same process:  
1. Formation of an ionic complex between a dipolar anionic  
substrate and a cation with a high cationic field or of a  
covalent complex between an amphoteric substrate and a ca-  
tion belonging to the transition metals. 2. The cation  
causes a redistribution of the charges, varying with the  
physicochemical properties of this cation in competition  
with the properties of the atoms of the coordinate. The ac-  
tive cation usually has six bonding directions depending on  
three perpendicular axes. Therefore, the attraction of this  
cation is exerted simultaneously on electrons  $\pi$  and  $\sigma$  of  
the atoms located on the planes formed by these axes. This  
is particularly effective on the coordination atoms. 4. In  
order for there to be rupture of a bond between two atoms  
A and B of the substrate, a dissociation of resonance must  
be produced only between these two atoms. But in the course  
of this dissociation of the resonance in the substrate mole-  
cule, only bond  $\pi$  is broken as would be the case if A and  
B remained negative or neutral. In the redistribution of  
the charges, the two atoms A and B of the bond under consid-  
eration have been dispossessed of a large part of their  
charge which results in a strong repulsion between these  
atoms. This repulsion causes a stretching of bond  $\sigma$  that

may go to the point of rupture. Therefore, there is rupture of the bond ( $\sigma + \pi$ ), producing two molecules.

Part of a theoretic study dealing with the rupture of certain bonds with a biological importance is given in this article: C=N (peptidic bond), C-C (in decarboxylation), P=O (ATP), P=N (phosphocreatine), O=O (by the respiratory enzymes).

The mechanism of the reaction within the transition complex is studied by calculating the differences in potential energy between the successive states.

A. The distribution of the charges on the atoms of the complex is studied in order to ascertain, if a rupture must occur, between which strongly positive consecutive atoms it may take place.

B. If possible, the dissociation energy of the bond A—B in the free molecule is calculated. In general, the bond order locates it between an ideal simple bond and double bond. In order to cause a rupture of the bond ( $\sigma + \pi$ ) it is, therefore, necessary to provide this amount of energy or when a drop in equivalent potential may occur in the transition complex.

C. But first, in the formation of the metal-substrate transition complex, a more or less large displacement of the mobile electrons is produced on the central cation, the effect of which is to stabilize the complex more or less. The difference in resonance energy between the original free molecule state and the metal-substrate transition complex state is calculated. This energy difference must be sufficient for the complex to form, but it must remain weak for the cation to be dissociated rapidly from the products formed after the reaction. Therefore, the weaker this energy difference, the more rapid is the reaction.

D. It is possible to calculate the resonance dissociation energy of bond A-B, if this bond is the only that loses its charges in the formation of the transition complex. It is obtained by the difference between the displacement energy in the metal-molecule substrate transition complex and the sum of the displacement energies in both parts of the complex after dissociation of the resonance on bond A=B. If this sum of the energies of the dissociated parts is lower than the energy of the molecule, dissociation occurs simultaneously in the complex.

E. Finally, it is possible to know the total dissociation ( $\sigma + \pi$ ) energy after the reaction, if the structure of the molecules that are formed is known. Most frequently it is a question of a hydrolysis.

1. Rupture of the Peptidic Bond. The compared action of active cations in the rupture of the peptidic bond has already been given (in Cahiers de Physique /Physics Notes/, in press). But the action of the active cations can be compared with the action of the inhibitory cations.

Four electrons are displaced on the N, C, O atoms of the peptidic bond in the molecule of free peptide. In the formation of a coordination complex with a metallic cation, a more or less large part of the N charge is displaced on the metallic cation, according to its electronegativity. N recovers part of this charge at the expense of the CN bond.

The two strongly positive C and N atoms repel each other, while the attraction between  $C^+$  and  $O^-$  increases. The length of bond CO decreases, while bond CN is lengthened.

The effect of an active cation  $Mn^{2+}$ , may be compared, with one that is very little active,  $Cr^{2+}$ , and with an inhibitor,  $Ag^{2+}$ .

#### A. Calculation of the charges:

	N	C	O	$M^{2+}$
Free molecule . . . . .	+0.56	+0.06	-0.675	--
$Cr^{2+}$ complex . . . . .	+0.367	+0.694	-0.723	-0.362
$Mn^{2+}$ complex . . . . .	+0.361	+0.698	-0.743	-0.311
$Ag^{2+}$ complex . . . . .	+1.104	+0.644	+0.252	-1.999

There is little difference in the distribution of charges between  $Cr^{2+}$  and  $Mn^{2+}$ . On the other hand,  $Ag^{2+}$  captures a pair of electrons, which makes the three atoms in the peptidic bond positive. The dissociation of the resonance, then, acts simultaneously on the two bonds, CN and CO.

B. The energy of the CN bond in the free molecule was calculated on the basis of the order of bonding. It is approximately 90 kg. cal. Therefore, the transition complex must cause a potential drop of at least 90 kg. cal. in the reaction.

C. The difference in energy that stabilizes the metal-substrate coordination complex is 50 29 kg. cal for  $\text{Cr}^{2+}$ , 35.76 kg. cal. with  $\text{Mn}^{2+}$  and 100 kg. cal. with  $\text{Ag}^{2+}$ . The least stable complex is the one formed with  $\text{Mn}^{2+}$ ; therefore, this is the one that is able to yield the greatest reaction speed.

D. The dissociation energy of the bond ( $\sigma + \pi$ ) is 64.4 kg. cal. with  $\text{Cr}^{2+}$ , 94.31 kg. cal. with  $\text{Mn}^{2+}$ , and 48.55 kg. cal. with  $\text{Ag}^{2+}$ .

The action of  $\text{Cr}^{2+}$ , therefore, is insufficient. The action of  $\text{Ag}^{2+}$ , as the calculation of the charges has shown us, is exerted simultaneously on both bonds, CN and CO. The two bonds are lengthened, but there is no rupture. Moreover, the cation that receives a pair of electrons forms a very stable complex.  $\text{Ag}^{2+}$  is able, therefore, to take the place of active cations and to form inert complexes that inhibit the reaction.

2. Decarboxylation. Activity of  $\text{Mg}^{2+}$  and  $\text{Mn}^{2+}$  on oxalacetic acid.

A. Calculation of the charges:

	O	CO	CO	CH <sub>2</sub>	CO	O	M <sup>2+</sup>
Free molecule	-0.22	+0.01	+0.30	-0.11	-0.03	+0.05	—
$\text{Mg}^{2+}$ complex	-0.22	+0.09	-0.72	+0.9	+0.03	+0.08	-0.15
$\text{Mn}^{2+}$ complex	-0.15	+0.14	-0.71	+0.9	+0.12	+0.11	-0.4

According to these results, the rupture must occur between  $\text{CH}_2$  and the carboxyl group.

B. In the formation of the transition complex, the displacement energy difference is 19 kg. cal. in the case of  $\text{Mg}^{2+}$  and 61.3 kg. cal. for  $\text{Mn}^{2+}$ .  $\text{Mg}^{2+}$ , therefore, yields a less stable complex, consequently a greater reaction speed than  $\text{Mn}^{2+}$ .

C. The value of 81 kg. cal. is given for C—C and 146 kg. cal. for C C. The dissociation energy of CC in the free molecule of oxalacetic acid is around 92 kg. cal.

D. A drop in potential of 94 kg. cal. is obtained with  $\text{Mg}^{2+}$  and 101.3 kg. cal. with  $\text{Mn}^{2+}$ , in the transition complex. One or the other of these cations, therefore,

must activate the decarboxylation of the oxalacetic acid.

3. Transphosphorylation. A study has been made on the kinases activated by  $Mg^{2+}$ . The calculation of the charges has been given as well as the resonance dissociation energy between the two terminal phosphate groups of ATP. It is 55.56 kg. cal.

In a complex in which ADP and  $P \sim$  are present, it is possible to reform the bond and the resonance between ADP and P to produce ATP by providing this energy in a coupled reaction.

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